AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listing of claims in the application.

1. (Currently Amended) A modified plasminogen activator inhibitor type-1 ("PAI-1") molecule comprising a helix D region, an A3 strand, an A4 strand and an A5 strand, ~~said molecule having an active form,~~ said molecule comprising the amino acid sequence which ~~has~~ is at least ~~about~~ 95% ~~similarity~~ identical to SEQ ID NO:2, ~~in which two or more amino acid residues are each substituted by~~ wherein SEQ ID NO:2 is modified with a substitution of an amino acid residue that contains a sulfhydryl group, such that ~~one or more~~ disulfide bridges are formed between or within said helix D region, A3 strand, A4 strand and/or A5 strand ~~of said modified PAI-1 molecule~~, and wherein ~~said active form of~~ said modified PAI-1 molecule has an *in vivo* half-life that is longer than the *in vivo* half-life of a corresponding wild-type PAI-1 ~~protein~~ molecule.

2. (Currently Amended) The modified PAI-1 molecule of claim 1 which has an ~~in vivo~~ *in vivo* half-life of over 3 hours, 6 hours, 10 hours, 20 hours, 50 hours, 60 hours, 70 hours, 90 hours, 100 hours, 150 hours, 200 hours, 10 days, 12 days, 16 days, 30 days, or 60 days.

3. (Canceled)

4. (Original) The modified PAI-1 molecule of claim 1 wherein said residue that contains a sulfhydryl group is cysteine.

5. (Currently Amended) A modified plasminogen activator inhibitor type-1 ("PAI-1 ") molecule ~~having an active form, in which two or more amino acid residues are each substituted by an amino acid residue that contains a sulfhydryl group, wherein: said active form of said modified PAI-1 molecule has an *in vivo* half-life that is longer than the *in vivo* half-life of a corresponding wild-type PAI-1 protein; and said two or more amino acid residues are selected from among~~ comprising the amino acid sequence of SEQ ID NO:2, wherein 1-6 amino acid residues of SEQ ID NO:2 is modified with a substitution of an amino acid residue that contains a sulfhydryl group at positions 31, 97, 192, 197, 347, and 355, said modified PAI-1 molecule has an *in vivo* half-life that is longer than the *in vivo* half-life of a

corresponding wild-type PAI-1 molecule ~~of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering~~.

6. (CurrentlyAmended) A modified plasminogen activator inhibitor type-1 ("PAI-1") molecule ~~having an active form in which two or more amino acid residues are each substituted by~~ comprising the amino acid sequence of SEQ ID NO:2, wherein SEQ ID NO:2 is modified with a substitution of an amino acid residue that contains a sulfhydryl group at positions (i) 31 and 97; (ii) 192 and 347; (iii) 197 and 355; (iv) 31, 97, 192, and 347; (v) 31, 97, 197, and 355; (vi) 192, 197, 347, and 355; or (vii) 31, 97, 192, 197, 347, and 355, and wherein: said ~~active form of said~~ modified PAI-1 molecule has an *in vivo* half-life that is longer than the *in vivo* half-life of a corresponding wild-type PAI-1 molecule ~~protein; and said two or more amino acid residues are selected from one or more pairs of amino acid positions including 31 and 97, 192 and 347, and 197 and 355 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering~~.

7. (Original) The modified PAI-1 molecule of claim 1 that further comprises one or more amino acid substitutions that are not substitutions with a sulfhydryl-containing residue.

8. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule inhibits urokinase plasminogen activator.

9. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule inhibits tissue plasminogen activator.

10. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule augments endogenous PAI-1 function.

11. (Currently Amended) A method of producing a modified plasminogen activator inhibitor type-1 molecule said method comprising:
(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule comprising a helix D region, an A3 strand, an A4 strand and an A5 strand, ~~said modified PAI-1 molecule having an active,~~ said molecule comprising the amino acid sequence which ~~has~~ is at least ~~about~~ 95% ~~similarity~~ identical to SEQ ID NO:2, ~~in which two or more amino~~

~~acid residues are each substituted by~~ wherein SEQ ID NO:2 is modified with a substitution of an amino acid residue that contains a sulfhydryl group, such that ~~one or more~~ disulfide bridges are formed between or within said helix D region, A3 strand, A4 strand, or A5 strand ~~of said modified PAI-1 molecule,~~ and wherein ~~said active form of~~ said modified PAI-1 molecule has an *in vivo* half-life that is longer than the *in vivo* half-life of a corresponding wild-type PAI-1 ~~protein~~ molecule; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

12. (Currently Amended) A method of producing a modified plasminogen activator inhibitor type-1 ("PAI-1") molecule, said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule ~~having an active form,~~ said molecule comprising the amino acid sequence of SEQ ID NO:2, wherein 1-6 amino acid residues of SEQ ID NO:2 is modified with a substitution of ~~which has at least about 95% similarity to SEQ ID NO:2 in which two or more amino acid residues are each substituted by~~ an amino acid residue that contains a sulfhydryl group at positions 31, 97, 192, 197, 347, and 355, wherein said active form of said modified PAI-1 molecule has an *in vivo* half life that is longer than the *in vivo* half-life of a corresponding wild-type PAI-1 molecule ~~protein~~; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule~~,~~

~~wherein said two or more amino acid residues are selected from among positions 31, 97, 192, 197, 347, and 355 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering~~.

13. (Currently Amended) A method of producing a modified plasminogen activated inhibitor type-1 ("PAI-1 ") molecule, said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule ~~having an active form,~~ said molecule comprising the amino acid sequence of SEQ ID NO:2, wherein SEQ ID NO:2 is modified with a substitution of ~~which has at least about 95% similarity to SEQ ID NO:2 in which two or more amino acid residues are each substituted by~~ an amino acid residue that contains a sulfhydryl group at positions (i) 31 and 97; (ii) 192 and 347; (iii) 197 and 355; (iv) 31, 97, 192, and 347; (v) 31, 97, 197, and 355; (vi) 192, 197, 347,

and 355; or (vii) 31, 97, 192, 197, 347, and 355, and wherein said ~~active form of said~~ modified PAI-1 molecule has an *in vivo* half life that is longer than the *in vivo* half-life of a corresponding wild-type PAI-1 ~~protein~~ molecule; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule~~,~~

~~wherein said two or more amino acid residues are selected from one or more pairs of amino acid positions including 31 and 97, 192 and 347, and 197 and 355 of the amino acid sequence of said wild-type PAI-1 protein using SEQ ID NO:2 for numbering~~.

14. (Currently Amended) A method of treating ~~a disease or disorder related to~~ aberrant angiogenesis in a subject in need thereof, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

15. (Withdrawn) A method of treating cancer in a subject suffering therefrom, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

16. (Withdrawn) The method of claim 15 wherein said cancer is selected from the group consisting of breast cancer, colon cancer, ovarian cancer, lung cancer, prostate cancer, melanoma, leukemia, lung cancer, skin cancer, pancreatic cancer, bladder cancer, sarcoma, and uterine cancer.

17. (Canceled).

18. (Canceled).

19. (Canceled)

20. (Canceled).

21. (Withdrawn) A method of treating uPA-mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

22. (Withdrawn) A method of treating tPA mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

23. (Original) A pharmaceutical composition comprising a therapeutically effective amount of the modified PAI-1 molecule of claim 1; and a pharmaceutically acceptable carrier.

24. (Currently Amended) The modified PAI-1 molecule of claim 1 wherein said A3 strand and A5 strand each comprises a top and a bottom part, said ~~one or more~~ disulfide bridges are formed linking said top part of A3 strand, said top part of A5 strand, said bottom part of A3 strand, said bottom part of A5 strand, and/or said helix D region.

25. (Canceled)

26. (Currently Amended) The modified PAI-1 molecule of ~~claim 1~~ claim 1 wherein ~~each said~~ SEQ ID NO:2 is modified with a substitution ~~by~~ of an amino acid residue that contains a sulfhydryl group ~~is~~ at ~~position~~ positions 10-40, 70-120, 150-220, 300-342, 343-350, and 351-400 of the amino acid sequence of ~~said wild-type PAI-1 protein using~~ SEQ ID NO:2 ~~for numbering~~.

27. (Currently Amended) The modified PAI-1 molecule of claim 1 wherein said ~~one or more~~ disulfide bridges are formed at ~~position~~ positions 29-32, 92-107, 180-197, 246-249, 341-353, 353-374, and 381-391 of ~~the amino acid sequence of said wild-type PAI-1 protein using~~ SEQ ID NO:2 ~~for numbering~~.

28. (Currently Amended) The modified PAI-1 molecule of claim 1 wherein said ~~one or more~~ disulfide bridges are formed at positions 10-40 and 70-120; and/or 150-220 and 300-

350 of ~~the amino acid sequence of said wild-type PAI-1 protein using~~ SEQ ID NO:2 ~~for numbering~~.

29. (Currently Amended) A modified PAI-1 molecule comprising ~~an~~ the amino acid sequence of SEQ ID NO:2 wherein amino acid residues at positions: (i) 31 and 97; (ii) 192 and 347; (iii) 197 and 355; (iv) 31, 97, 192, and 347; (v) 31, 97, 197, and 355; (vi) 192, 197, 347 and 355; or (vii) 31, 97, 192, 197, 347, and 355, are substituted with amino acid residues that contain a sulfhydryl group.

30. (Previously Presented) A method of producing a modified plasminogen activator inhibitor type-1 ("PAI-1") molecule said method comprising:
(a) introducing into a cell a nucleic acid molecule encoding ~~a~~ the modified PAI-1 molecule of claim 28; and
(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

31. (Previously Presented) A method of producing a modified plasminogen activator inhibitor type-1 ("PAI-1") molecule said method comprising:
(a) introducing into a cell a nucleic acid molecule encoding ~~a~~ the modified PAI-1 molecule of claim 29; and
(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.